

CLAIMS

1. The method of producing dosage units of a solid drug form containing as the active substance warfarin sodium salt in an amount of 1 to 10 mg and having high degree of content uniformity meeting Bergum criterion, characterized in that a required amount of an aqueous solution of warfarin sodium salt and/or its clathrate which optionally contains in the dissolved state one of pharmaceutically acceptable excipients co-forming the solid drug form to be prepared but not all the pharmaceutically acceptable excipients co-forming the solid drug form to be prepared, is brought into contact with solid particles of at least one pharmaceutically acceptable excipient co-forming the solid drug form to be prepared, whereupon optionally the particles are dried and optionally mixed with the required amount of solid particles of the remaining pharmaceutically acceptable excipients co-forming the solid drug form to be prepared, and the thus-obtained particulate mixture is formulated into dosage units of the solid drug form.
2. The method according to claim 1, characterized in that the bringing into contact of an aqueous solution of warfarin sodium salt and/or its clathrate with solid particles of at least one pharmaceutically acceptable excipient is performed by spraying this solution onto these solid particles.
3. The method according to claim 1 or 2, characterized in that the aqueous solution of warfarin sodium salt and/or its clathrate contains 1 to 50 % by weight, preferably 8 to 35 % by weight, of warfarin sodium salt and/or its clathrate, based on the weight of the solution.
4. The method according to any of claims 1 to 3, characterized in that the aqueous solution of warfarin sodium salt and/or its clathrate contains, beside water, solely warfarin sodium salt and/or its clathrate.
5. The method according to any of claims 1 to 4, characterized in that the solid particles of at least one pharmaceutically acceptable excipient intended for bringing into contact with aqueous solution of warfarin sodium salt and/or its clathrate, have such particle distribution that the size of at least 90 % of these particles is greater than 40 micrometers, the size of at most 10 % of these particles is greater than 250 micrometers, and 100 % of these particles are of a size not exceeding 300 micrometers.

6. The method according to any of claims 1 to 5, characterized in that the pharmaceutically acceptable ingredients are selected from a group consisting of a hydrophilic sugar, preferably sucrose, sorbitol, mannitol or lactose, natural or modified starch and cellulose, the most preferred being a mixture of lactose and microcrystalline cellulose in a weight ratio 10 : 5 to 11 : 5.
7. The method according to any of claims 1 to 6, characterized in that the solid particles of at least one pharmaceutically acceptable excipient, intended for bringing into contact with aqueous solution of warfarin sodium salt and/or its clathrate, contain added solid particles of a pharmaceutically acceptable excipient of a specific surface area of at least $150 \text{ m}^2 \cdot \text{g}^{-1}$ in an amount of 0.1 to 2 % by weight based on the total weight of solid particles of at least one pharmaceutically acceptable excipient and the said added ingredient intended for bringing into contact with aqueous solution of warfarin sodium salt and/or its clathrate, preferably added colloidal silicon oxide, in an amount of 0.5 % by weight based on the total weight of solid particles of at least one pharmaceutically acceptable excipient and the said added ingredient intended for bringing into contact with aqueous solution of warfarin sodium salt and/or its clathrate.
8. The method according to any of claims 1 to 7, characterized in that the mixture of solid, optionally dried particles, obtained after spraying an aqueous solution of warfarin sodium salt and/or its clathrate onto solid particles of at least one pharmaceutically acceptable excipient, is mixed with at least one pharmaceutically acceptable lubricant such as preferably magnesium stearate, zinc stearate, aluminium stearate, colloidal silicon oxide, stearic acid, sodium stearyl fumarate, polyethylene glycol or sodium lauryl sulfate, used in an amount of 0.1 to 10 % by weight based on the weight of the obtained mixture, preferably with magnesium stearate used in an amount of 1 % by weight based on the weight of the mixture obtained.
9. The method according to any of claims 1 to 8, characterized in that the mixture of solid, optionally dried particles, obtained after spraying an aqueous solution of warfarin sodium salt and/or its clathrate onto solid particles of at least one pharmaceutically acceptable excipient, is mixed with at least one pharmaceutically acceptable disintegrant such as preferably ultraamylopectin, sodium salt of crosslinked carboxymethylcellulose or crosslinked polyvinylpyrrolidone, used in an amount of 1 to

7 % by weight, based on the weight of the mixture obtained, preferably with sodium salt of crosslinked carboxymethylcellulose, used in an amount of 2 % by weight based on the weight of the mixture obtained.

10. The method according to any of claims 1 to 9, characterized in that the obtained particulate mixture is formulated into dosage units of solid drug form by filling into capsules and/or sachets, and/or by pressing to tablets.